DOI:
10.1200/JCO.2015.65.2875

VOLUME 34 · NUMBER 13 · MAY 1, 2016

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Surgical Proficiency Gain and Survival After Esophagectomy for Cancer

Sheraz R. Markar, Hugh Mackenzie, Pernilla Lagergren, George B. Hanna, and Jesper Lagergren

Sheraz R. Markar, Hugh Mackenzie, and George B. Hanna, Imperial College London; Jesper Lagergren, King's College London, London, United Kingdom; and Sheraz R. Markar, Pernilla Lagergren, and Jesper Lagergren, Karolinska Institutet, Sweden.

Published online ahead of print at www.jco.org on March 7, 2016.

Funded by the Swedish Research Council and the Swedish Cancer Society. S.R.M. is supported by the National Institutes of Health Research.

Authors' disclosures of potential conflicts of interest are found in the article online at www.jco.org. Author contributions are found at the end of this article.

Corresponding author: Jesper Lagergren, PhD, Department of Molecular Medicine and Surgery, Karolinska Institutet, NS 67, 2nd Floor, 171 76 Stockholm, Sweden; e-mail: jesper.lagergren@ki.se.

0732-183X/16/3413w-1528w/$20.00

DOI: 10.1200/JCO.2015.65.2875

ABSTRACT

Purpose
We aimed to identify the presence and length of esophagectomy proficiency gain curves in terms of short- and long-term mortality for esophageal cancer.

Patients and Methods
Patients who underwent esophagectomy for esophageal cancer between 1987 and 2010 with follow-up until 2014 were identified from a well-established, population-based, nationwide Swedish cohort study. Proficiency gain curves were created by using risk-adjusted cumulative sum analysis for 30-day, 90-day, 1-year, 3-year, and 5-year all-cause and disease-specific mortality measures. Similarly, the proficiency gain curves for lymph node harvest, resection margin status, and reoperation incidence were assessed as performance-contributing factors to the observed changes in long-term survival.

Results
Esophagectomies in 1,821 patients with esophageal cancer were conducted by 139 surgeons. The change-point in proficiency gain curve for all-cause 30-day mortality was early, at 15 cases, when mortality decreased from 7.9% to 3.1% ($P < .001$). Later change-points, which ranged from 35 to 59 cases, were observed for 1-, 3- and 5-year mortality rates, for which all-cause mortality decreased from 34.9% to 27.7% ($P = .011$), from 47.4% to 41.5% ($P = .049$), and from 31.4% to 19.1% ($P = .009$), respectively. Similar change-points were observed in disease-specific mortality at 1 and 3 years. There was a continuous increase in lymph node harvest, which did not plateau. Also, change-points were observed for resection margin with tumor involvement at 17 cases, with a reduction from 20.9% to 15.2% ($P = .004$), and for reoperation rate at 55 cases, with a reduction from 12.6% to 5.0% ($P < .001$).

Conclusion
The gain of proficiency in esophagectomy for cancer is associated with measurable changes in short- and long-term mortality results. These findings indicate a need for structured national training and mentorship programs for esophageal cancer surgery.

J Clin Oncol 34:1528-1536. © 2016 by American Society of Clinical Oncology

INTRODUCTION

Esophageal cancer is the eighth most common cancer globally (annually affecting 482,300 people), and its incidence is increasing.[1-3] The overall European pooled relative 1-year and 5-year survival rates are 33.4% (95% CI, 32.9% to 33.9%) and 9.8% (95% CI, 9.4% to 10.1%), respectively.[4] Centralization of esophagectomy to high-volume centers in recent years has rendered improvements in short-term complications, postoperative mortality,[5-7] and long-term survival; surgeon volume is of greater importance than hospital volume.[8,9]

The introduction of minimal-access surgery has highlighted the effect of surgeons gaining proficiency in new techniques. Typically, studies that addressed surgeon proficiency gain curves in relation to gastrointestinal cancer have focused on short-term outcomes.[10-12] Few studies have considered the changes in long-term survival as surgeons gain proficiency in laparoscopic gastrectomy,[13,14] laparoscopic hemicolectomy,[15] and open esophagectomy.[16] These studies often describe the practice of high-volume surgeons in high-volume centers and, therefore, do not reflect the average proficiency gain curve. A study on the national proficiency gain curve in the United Kingdom in minimal-access surgery has described measurable effects upon short-term clinical outcomes after esophageal and colorectal cancer resections as surgeons gain proficiency.[17] However, to date, no study has been undertaken to assess the impact of proficiency gain on long-term mortality after cancer resection at a national level. The objective of this study was to estimate esophagectomy proficiency gain curves in terms of short- and long-term mortality in esophageal cancer in a nationwide and comprehensive cohort of patients.

PATIENTS AND METHODS

Design

The cohort used for this study has been described in detail elsewhere.[9,18] In brief, this Swedish nationwide cohort study included 98% of all patients with esophageal cancer treated with a curative intent between 1987 and 2010, with follow-up until November 2014. From the Swedish Cancer Registry, patients with a diagnosis of esophageal cancer (150.0, 150.8, or 150.9) were identified according to the seventh edition of the International Classification of Diseases (ICD7). This registry has 98% nationwide coverage of esophageal cancer cases.[19,20] Patients with esophageal cancer who underwent esophagectomy were identified from the Swedish Patient Registry, which has an excellent positive identification rate (99.6%) for esophageal surgery.[21] The Patient Registry also provided data about patient medical comorbidities and reoperation.[21] The comorbidities were classified according to the well-validated Charlson comorbidity score system.[22] The Swedish Causes of Death Registry was used to provide accurate data about the dates and causes of death. If the diagnosis of esophageal cancer was listed as a cause of death, then mortality was defined as disease specific. The Swedish personal identity number, assigned to each Swedish resident at birth or immigration, was used to link data between registries and in the identification of individual medical records. Medical records that contained operation notes and histopathological reports of the cohort members were retrieved from all Swedish hospitals where esophageal cancer surgery was performed. Clinical data were collected through a nationwide Swedish clinical network established in the mid-1990s.[23] Data about neoadjuvant therapy, names of the surgeons, tumor pathologic stage, histologic subtype, and lymphadenectomy were obtained from these individual patient records. The accuracy of histopathological review has been previously described; two researchers independently reviewed 100 records and demonstrated high accuracy with > 90% concordance.[24] Neoadjuvant therapy was predominantly used in more recent years and, when used, was typically a combination of chemotherapy and radiotherapy. Tumor stage was classified according to the TNM classification of the International Union Against Cancer (UICC).[25] Only open transthoracic esophageal resection was studied, and intrathoracic anastomosis was most commonly used (95%). Minimally invasive esophagectomy was performed in < 2% of cases in Sweden during the study period, which did not permit additional analysis of the proficiency gain curve. The regional ethical review board in Stockholm, Sweden, approved the study.

Outcomes

The outcomes were 30-day, 90-day, 1-year, 3-year, and 5-year all-cause and disease-specific mortality. To exclude the effect of earlier mortality on the longer-term results, 90-day mortality was calculated from 30 to 90 days; 1-year mortality, from 90 days to 1-year; 3-year mortality, from 1 year to 3 years; and 5-year mortality, from 3 years to 5 years. Lymph node yield, reoperation, and resection margin status (R1/2) were examined as explanatory performance-related variables to any changes in long-term survival. R1 or R2 refer to microscopic or macroscopic presence of tumor at the resection margin, respectively.

Statistical Analysis

Follow-up of patients ended at death, emigration, or the end of the study period (November 2014), whichever occurred first. According to the unique anonymized surgeon codes within the database, the first case in each surgeon case series was assigned case one, and subsequent case numbers were assigned according to ascending date order. Risk-adjusted cumulative sum (RA-CUSUM) curves were created to define the proficiency gain curve for each mortality outcome from esophagectomy.[26] Risk prediction models for the binary outcomes were created by using logistic regression models. Potential confounding factors included in the models were age (continuous variable), sex (male or female), tumor histologic subtype (adenocarcinoma or squamous cell carcinoma), pathologic stage (stage I, II, III, or IV), use of neoadjuvant therapy (yes or no), and individual preoperative comorbidities (yes or no). The risk prediction models were used to calculate the predicted probability of each outcome in each case (the expected survival or mortality; Appendix Table A1, online only). The curves plot the cumulative difference between the observed and expected mortality/survival (ie, CUSUM O [minus] E, on the y-axis) according to the risk-adjustment model. This difference was calculated using the CUSUM equation $S_i = S_{i-1} + (\Sigma_i - \Sigma_R)$; $S_0 = 0$. S_i is the cumulative sum, Σ_i is the sum of events at procedure number i, and Σ_R is the sum of expected events at procedure number i. RA-CUSUM curves were also examined for lymph node harvest, positive resection margin, and reoperation rates. On the basis of this equation, the curve increases if the observed mortality/survival exceeds the expected mortality/survival and vice versa.

It was expected that there would be an inverse relationship between experience and mortality. Therefore the change-points were identified as the maximal deflection of the curve from 0; the significance of the change-points was analyzed by comparing the relevant outcomes before and after. Binomial outcomes were compared with the χ^2 test, and continuous

Table 1. Demographics of Patients Who Underwent Esophagectomy From 1987 to 2010

Variable	No. (%) of Patients
Age, years	
Median	66
Range	18-89
Male sex	1,361 (74.7)
Ischemic heart disease	150 (8.2)
Congestive cardiac failure	96 (5.3)
Peripheral vascular disease	64 (3.5)
Cerebrovascular disease	107 (5.9)
Chronic obstructive pulmonary disease	199 (10.9)
Diabetes	146 (8.0)
Liver disease	28 (1.5)
Renal disease	21 (1.2)
Charlson comorbidity score[22]	
0-1	1,440 (79.1)
2-4	362 (19.9)
≥ 5	19 (1)
Histologic tumor subtype	
Adenocarcinoma	792 (43.5)
Squamous cell carcinoma	1,024 (56.2)
Pathologic tumor stage	
0	177 (9.7)
I	245 (13.5)
II	662 (36.4)
III	582 (32.0)
IV	140 (7.7)
Missing	15 (0.8)
Neoadjuvant therapy	587 (32.2)
Missing	2 (0.1)

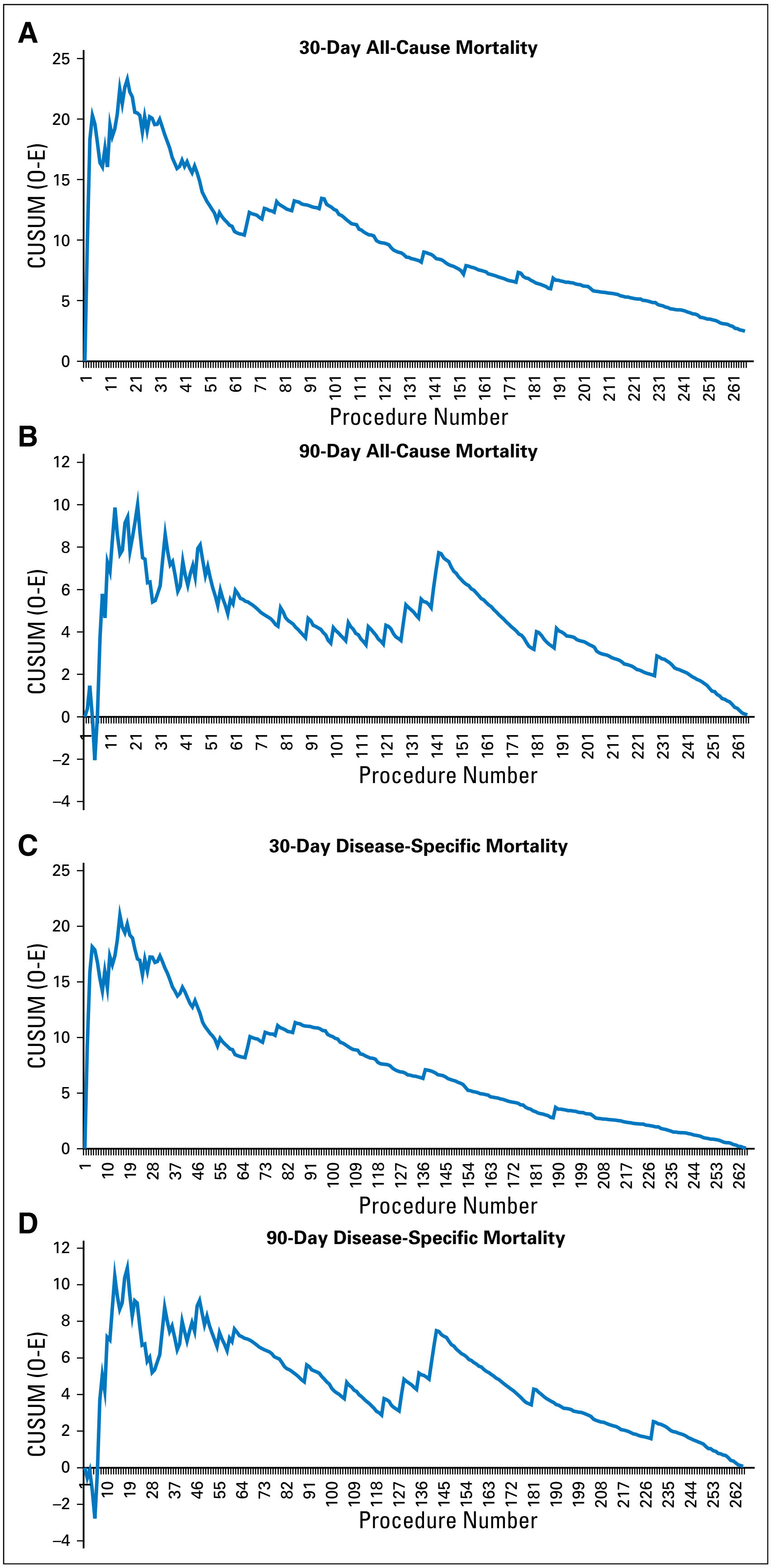

Fig 1. Proficiency gain curves for (A) 30-day all-cause mortality from esophagectomy for cancer with a significant change-point at 15 cases with a reduction from 7.9% to 3.1% ($P < .001$); (B) 90-day all-cause mortality from esophagectomy for cancer with a nonsignificant change-point at 22 cases with a reduction from 7.3% to 5.2% ($P = .079$); (C) 30-day disease-specific mortality from esophagectomy for cancer with a significant change-point at 15 cases with a reduction from 7.3% to 2.5% ($P < .001$); and (D) 90-day disease-specific mortality from esophagectomy for cancer with a significant change-point at 18 cases with a reduction from 7.1% to 4.3% ($P = .043$). Abbreviations: E, expected; O, observed.

outcomes were compared with the Mann-Whitney *U* test. A threshold of significance was set at $P < .05$.

RESULTS

This study included 1,821 patients with esophageal cancer who underwent esophagectomy, and these operations were performed by a total of 139 surgeons. The median number of cases performed by the surgeons was 16, and the interquartile range was six to 46 cases; the most experienced surgeon had performed 262 cases. The median follow-up time was 491 days. The median age at surgery was 66 years, a high proportion of patients (74.7%) were men, and there was a relatively low rate of medical comorbidities (Charlson score ≤ 1 in 79.1% of patients). There was a greater proportion of squamous cell cancers (56.2%) than adenocarcinomas (43.5%). The majority of tumors were pathologic stage II (36.4%) or III (32%), and 32.2% of patients received neoadjuvant therapy (Table 1). Among this cohort, 1,272 patients (69.9%) had no cancer in the resection margin (R0), whereas 281 patients (15.4%) had cancer in the margin (R1/R2); 268 patients (14.7%) had missing margin data.

Proficiency Gain Curve Analysis

Short-term mortality. The 30-day and 90-day measures were short-term mortality data (Fig 1). The incidences of 30-day and 90-day all-cause mortality for the cohort were 5.3% and 6.4%, respectively (Table 2). There were change-points in the proficiency gain curves at 15 cases and 22 cases, respectively, at which point the 30-day all-cause mortality decreased from 7.9% to 3.1% ($P < .001$; Fig 1A) and the 90-day all-cause mortality decreased from 7.3% to 5.2% ($P = .079$; Fig 1B).

The incidences of 30-day and 90-day disease-specific mortality were 4.7% and 5.7%, respectively (Table 2). The RA-CUSUM analysis for 30-day disease-specific mortality showed a change-point at 15 cases, with a reduction from 7.3% to 2.5% ($P < .001$; Fig 1C). The RA-CUSUM analysis for 90-day disease-specific mortality showed a significant change-point at 18 cases, and the reduction in 90-day disease-specific mortality decreased from 7.1% to 4.3% ($P = .017$; Fig 1D).

Long-term mortality. The 1-, 3- and 5-year measures were long-term mortality data (Figs 2 and 3). RA-CUSUM analysis of 1-year all-cause mortality showed a significant change-point at 53 cases, with a reduction from 34.9% to 27.7% ($P = .011$; Fig 2A). A similar significant change-point was seen for 3-year all-cause mortality at 35 cases, with a reduction from 47.4% to 41.5% ($P = .049$; Fig 2B). The RA-CUSUM analysis of 5-year all-cause mortality showed a significant change-point at 59 cases, with a reduction from 31.4% to 19.1% ($P = .006$; Fig 2C).

RA-CUSUM analysis of 1-year disease-specific mortality showed a significant change-point at 53 cases, with a reduction from 31.8% to 24.7% ($P = .01$; Fig 3A). Similarly, a change-point was seen for 3-year disease-specific mortality at 38 cases, with a reduction from 39.4% to 32.8% ($P = .034$; Fig 3B). There was no apparent proficiency gain curve seen with 5-year disease-specific mortality (Table 2; Fig 3C).

Lymph Node Harvest, Resection Margin Status, and Reoperation Incidence

There was a marked increase in lymph node harvest, although it was not possible to define an exact change point because of the smooth nature of the curve (Fig 4A). The RA-CUSUM analysis for R1/2 resection margin status showed a significant change-point at 17 cases, with a reduction from 20.9% to 15.2% ($P = .004$; Fig 4B). RA-CUSUM analysis for reoperation showed a significant change-point at 55 cases, with a reduction from 12.6% to 5% ($P < .001$; Fig 4C).

DISCUSSION

This study indicates that resection of esophageal cancer has a proficiency gain curve with a measurable evolution in both short- and long-term mortality. The change-points in proficiency gain curve were earlier for short-term mortality (30- and 90-day mortality), which ranged from 15 to 22 cases, than the later

Table 2. Outcomes Before and After Change-Points in Proficiency Gain Curves for All-Cause and Disease-Specific Mortality Results After Esophagectomy for Cancer

Mortality time point	Proficiency Gain Curve Change-Point (No. of cases)	% (No./Total No.) With Outcome: Overall	Prior to Change-Point	After Change-Point	Change-Point *P*
All-cause					
30-day	15	5.3 (94/1,761)	7.9 (65/825)	3.1 (29/936)	< .001
90-day	22	6.4 (107/1,667)	7.3 (70/955)	5.2 (37/712)	.079
1-year	53	33.3 (520/1,562)	34.9 (422/1,208)	27.7 (98/354)	.011
3-year	35	45.4 (474/1,044)	47.4 (328/692)	41.5 (146/352)	.049
5-year	59	28.6 (163/570)	31.4 (138/439)	19.1 (25/131)	.006
Disease-specific					
30-day	15	4.7 (83/1,761)	7.3 (60/825)	2.5 (23/936)	<.001
90-day	18	5.7 (96/1,678)	7.1 (60/850)	4.3 (36/828)	.017
1-year	53	30.1 (477/1,583)	31.8 (388/1,222)	24.7 (89/361)	.010
3-year	38	37.2 (412/1,107)	39.4 (294/747)	32.8 (118/360)	.034
5-year	No change-point	NA	NA	NA	NA

Abbreviation: NA, not available.

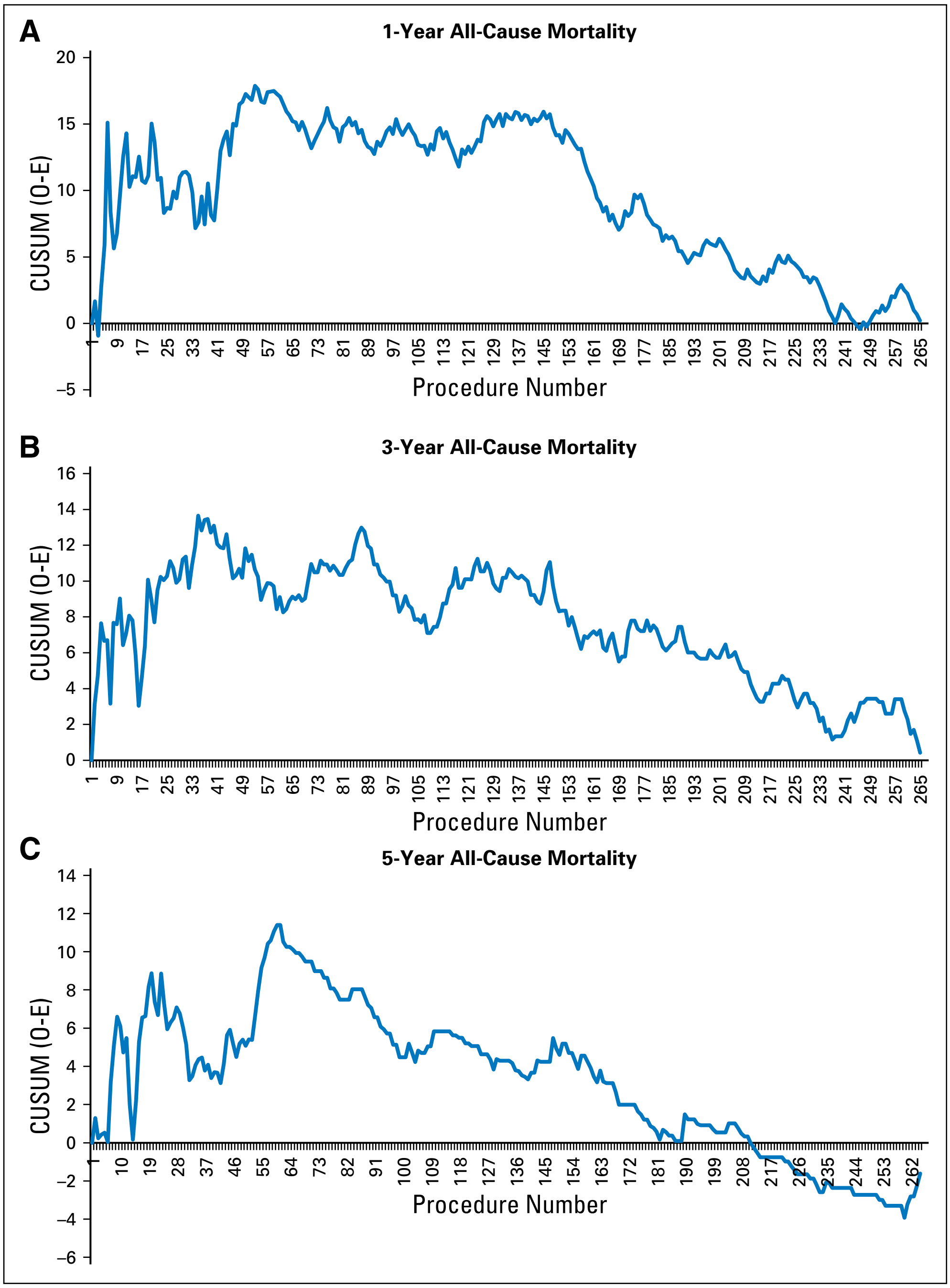

Fig 2. Proficiency gain curves for (A) 1-year all-cause mortality from esophagectomy for cancer with a significant change-point at 53 cases with a reduction from 34.9% to 27.7% (*P* =.011); (B) 3-year all-cause mortality from esophagectomy for cancer with a significant change-point at 35 cases with a reduction from 47.4% to 41.5% (*P* = .049); and (C) 5-year all-cause mortality from esophagectomy for cancer with a significant change-point at 59 cases with a reduction from 31.4% to 19.1% (*P* = .006). Abbreviations: E, expected; O, observed.

change-points for long-term mortality (1-, 3- and 5-year mortality) that ranged from 35 to 59 cases.

The relatively short length of the proficiency gain curve for short-term mortality parallels published literature from single institutions in open esophagectomy[16] and a national study for minimally invasive esophagectomy in England.[17] There was a 5% reduction in 30-day mortality observed during the proficiency gain curve, which represents a non-negligible degree of patient harm as surgeons gain operative experience. Importantly, the proficiency gain curve for long-term mortality was longer. The initial focus of independent surgeon practice is likely to be short-term outcome and, in particular, the 30-day mortality. When early mortality has been reduced to an acceptable level and when the surgeon gains the technical confidence in performing the procedure, surgeons then can refine their techniques and improve the quality of the resection, which will result in better long-term survival.

There are several potential mechanisms that might contribute to the findings about the learning curve in relation to long-term survival. Although a higher lymph node yield with more experience might be one such mechanism, a recent study that was based on the same cohort as the present study showed that lymph node harvest was not an independent predictor of survival.[18] Nevertheless, lymph node harvest in the current

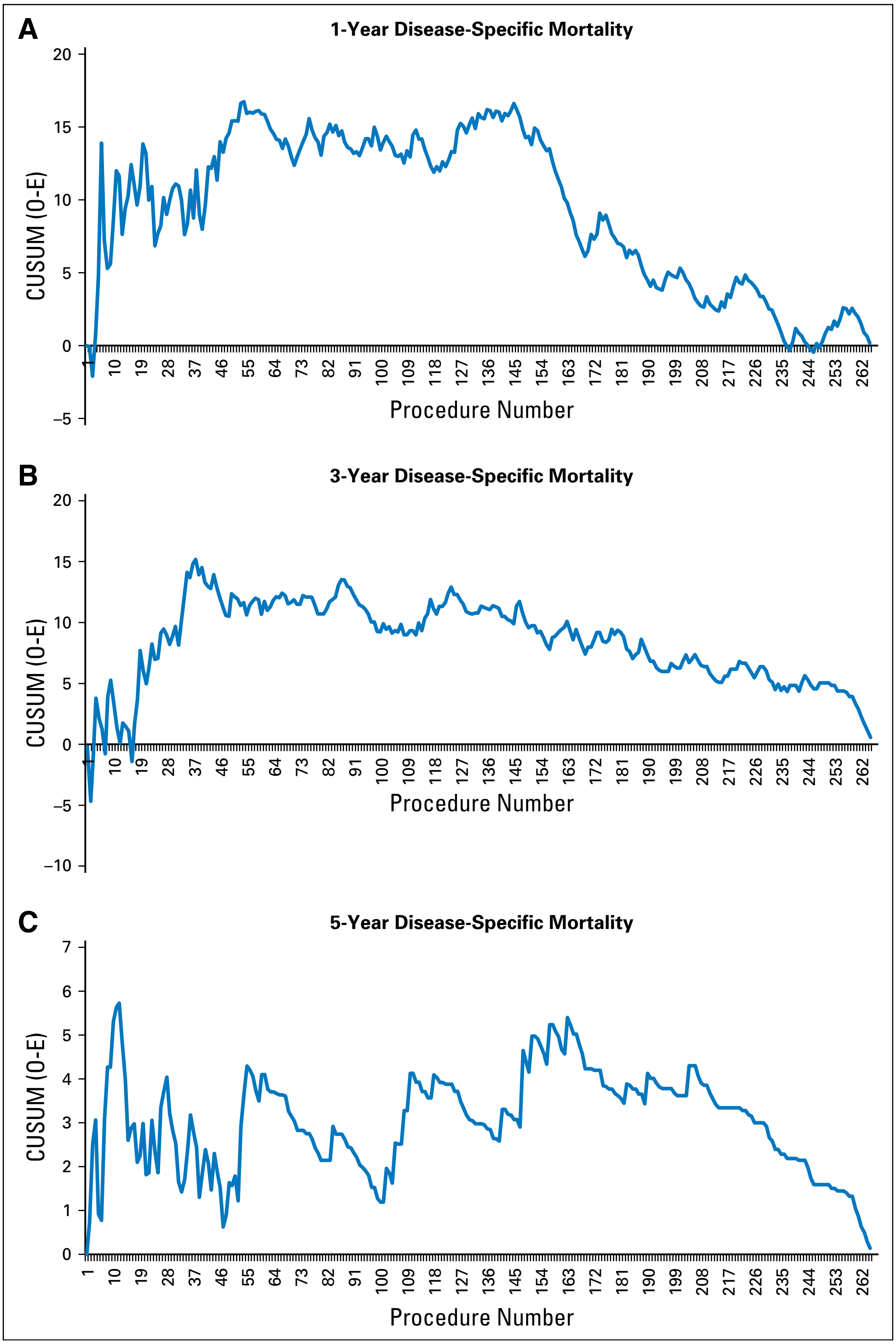

Fig 3. Proficiency gain curves for (A) 1-year disease-specific mortality from esophagectomy with a significant change-point at 53 cases with a reduction from 31.8% to 24.7% (P = .01); (B) 3-year disease-specific mortality from esophagectomy for cancer with a significant change-point at 38 cases with a reduction from 39.4% to 32.8% (P = .034); and (C) 5-year disease-specific mortality from esophagectomy for cancer showing no significant pattern. Abbreviations: E, expected; O, observed.

study might be a marker of improved oncologic surgical quality with proficiency gain. The finding that cancer involvement in the resection margin was overrepresented among surgeons in the beginning of an esophagectomy career might well contribute to the higher longer-term mortality rates, because margin involvement is a prognostic factor.[27] Finally, reductions in reoperation incidence parallel findings from a study that was based on the present database, which suggests that reoperation affects long-term survival after esophagectomy.[28]

Gaining experience at the expense of patient safety or long-term survival is unacceptable, and every effort must be made to overcome the proficiency gain curve for both short- and long-term mortality results. This study showed proficiency gain in an established operation. Open esophagectomy is not a newly

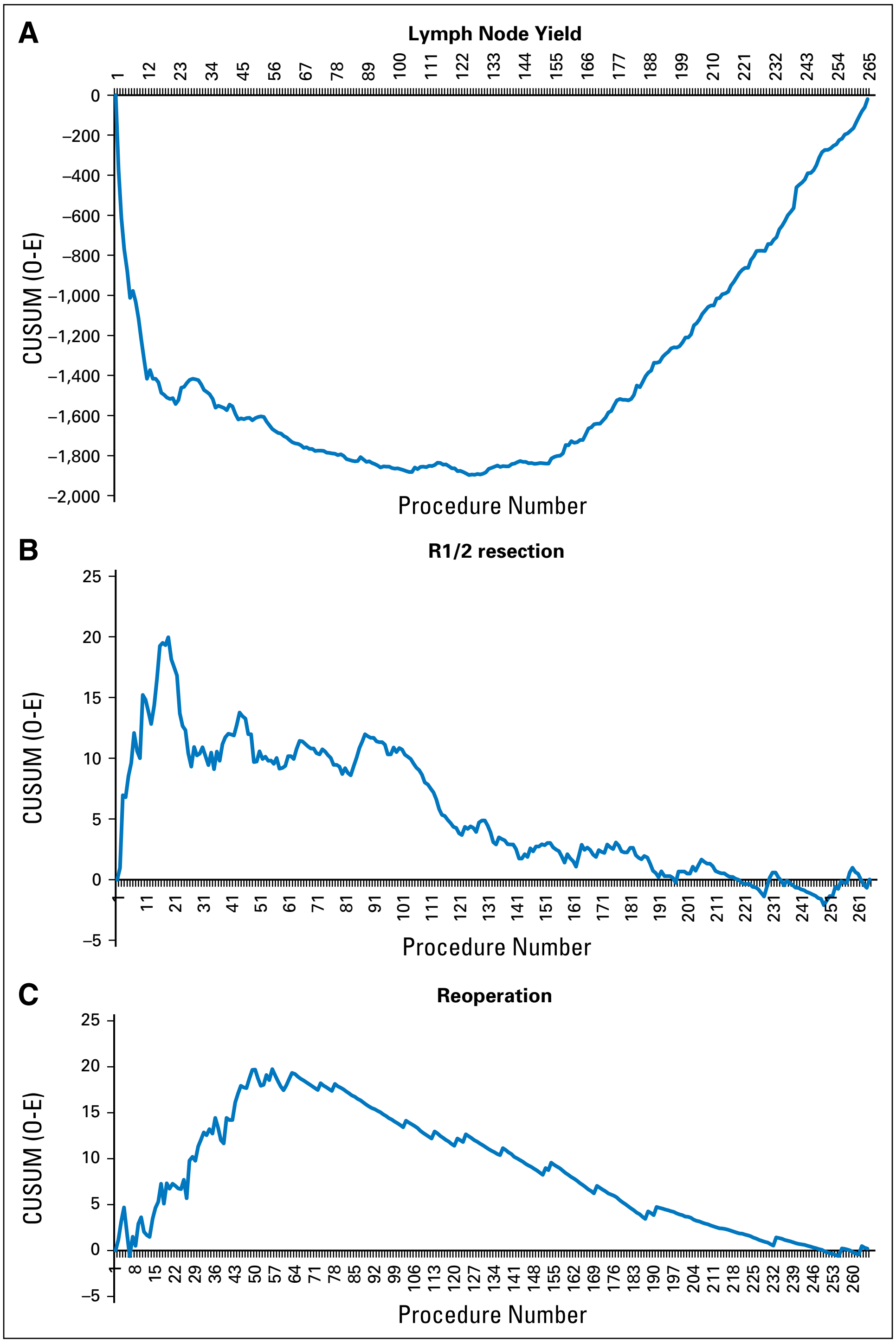

Fig 4. Proficiency gain curves for lymph node harvest from esophagectomy for cancer showing (A) a continuous increase in lymph node harvest with greater case load; (B) R1/2 resection margin from esophagectomy for cancer showing a significant change-point at 17 cases with a reduction from 20.9% to 15.2% (P = .004); and (C) reoperation from esophagectomy for cancer showing a significant change-point at 55 cases with a reduction from 12.6% to 5.0% (P < .001). Abbreviations: E, expected; O, observed.

introduced procedure; a proficiency gain curve has been traditionally observed during the dissemination of a technique, and minimal-access surgery is the typical example.[17] Nevertheless, open esophagectomy is a technically demanding procedure in which there is much to learn and optimize before proficiency can be achieved. To shorten the proficiency gain curve and to minimize avoidable harm to patients, we believe in two main strategies. The first is to base surgical training on structured programs that have a competency-based assessment before embarking on independent practice.[29,30] Such a strategy can replace the current training system on the basis of the number of procedures, the years of training, and the subjective opinions of trainers. Second, this competency-based training curriculum should be followed by a mentorship and continual technical proficiency scheme to support specialists during the initial phase of independent practice. A good example of such a structured training program was observed with the National

Training Program for Laparoscopic Colorectal Surgery in England. This program was a government initiative that facilitated the training of surgeons in a structured, competency-based program that shortened the proficiency gain curve and reduced patient harm during the process of surgical learning.[29-31]

Methodological advantages of the current study include the population-based design with complete and unbiased inclusion of patients who had undergone esophagectomy for esophageal cancer in Sweden since 1987. Moreover, the clinical data collection combined with data available in the well-maintained registers allowed us to perform this analysis and to adjust for several potential confounding factors. Furthermore, the Swedish system with nationwide and complete population registers made it possible to observe all patients, without loss to follow-up. Finally, the large sample size improved the statistical power and counteracted chance errors.

There are also limitations associated with retrospective observational studies such as this. Typically, national database studies are limited by the quality of data entry; however, the data set used for this study has high accuracy in the correct identification of patients who underwent esophagectomy for cancer and has a strong correlation with pathology, including tumor stage. Moreover, the medical records were retrieved and reviewed, which made it possible to have detailed clinical data, including the surgeon name as a variable required for this study. Additional unmeasured surgical factors may have improved the oncologic quality and long-term survival. Although the study period began in 1987 and, therefore, represents one of the oldest existing national data sets for esophagectomy, it is conceivable that a minority of surgeons may have begun operating before 1987; thus, the early part of their proficiency gain curve may not have been captured. The study period is rather long; therefore, it is conceivable that improvements in other areas over time, including clinical staging that led to better patient selection for surgical intervention or improvements in neoadjuvant therapy regimens and enhanced recovery protocols, may have contributed to the improvement in short- and long-term outcomes during the surgical proficiency gain. However, it is important to note that case 1 was taken by surgeons at the start of their practice and that the practices showed temporal variations throughout the study period; despite the presumed improvements seen in other areas, there was a quantifiable proficiency gain curve in terms of short- and long-term survival. Finally, although risk adjustment in CUSUM analysis did include pathologic stage, histologic subtype, use of neoadjuvant therapy, and patient demographics, including comorbidities, there may have been additional unknown confounding factors that may have contributed to the observed changes in survival.

In conclusion, to our knowledge, this is the first study to evaluate the change in long-term mortality at a national level as the surgeon gains proficiency in performing open esophagectomy for cancer, and shows that the length of the proficiency gain curve was shorter for short-term than for long-term mortality. The adverse impact of proficiency gains upon patient outcomes may be negated with competency-based training programs before surgeons embark on independent practice that are followed by a mentoring and a continual proficiency scheme during the initial practice as specialists.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at www.jco.org.

AUTHOR CONTRIBUTIONS

Conception and design: Sheraz R. Markar, Pernilla Lagergren, George B. Hanna, Jesper Lagergren
Collection and assembly of data: Sheraz R. Markar, Pernilla Lagergren, George B. Hanna, Jesper Lagergren
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors

REFERENCES

1. Jemal A, Bray F, Center MM, et al: Global cancer statistics. CA Cancer J Clin 61:69-90, 2011

2. Siegel R, Naishadham D, Jemal A: Cancer statistics, 2012. CA Cancer J Clin 62:10-29, 2012

3. Blot WJ, Devesa SS, Kneller RW, et al: Rising incidence of adenocarcinoma of the esophagus and gastric cardia. JAMA 265: 1287-1289, 1991

4. Gavin AT, Francisci S, Foschi R, et al: Esophageal cancer survival in Europe: A EUROCARE-4 study. Cancer Epidemiol 36:505-512, 2012

5. Munasinghe A, Markar SR, Mamidanna R, et al: Is it time to centralize high-risk cancer care in the United States? Comparison of outcome of esophagectomy between England and United States. Ann Surg 262:79-85, 2015

6. Markar SR, Karthikesalingam A, Thrumurthy S, et al: Volume-outcome relationship in surgery for esophageal malignancy: Systematic review and meta-analysis 2000-2011. J Gastrointest Surg 16: 1055-1063, 2012

7. Coupland VH, Lagergren J, Lüchtenborg M, et al: Hospital volume, proportion resected and mortality from esophageal and gastric cancer: A population-based study in England, 2004-2008. Gut 62:961-966, 2013

8. Brusselaers N, Mattsson F, Lagergren J: Hospital and surgeon volume in relation to long-term survival after esophagectomy: Systematic review and meta-analysis. Gut 63:1393-1400, 2014

9. Derogar M, Sadr-Azodi O, Johar A, et al: Hospital and surgeon volume in relation to survival after esophageal cancer surgery in a population-based study. J Clin Oncol 31:551-557, 2013

10. Miskovic D, Ni M, Wyles SM, et al: Learning curve and case selection in laparoscopic colorectal surgery: Systematic review and international multicenter analysis of 4852 cases. Dis Colon Rectum 55: 1300-1310, 2012

11. Tapias LF, Morse CR: Minimally invasive Ivor Lewis esophagectomy: Description of a learning curve. J Am Coll Surg 218:1130-1140, 2014

12. Zhou D, Quan Z, Wang J, et al: Laparoscopic-assisted versus open distal gastrectomy with D2 lymph node resection for advanced gastric cancer: Effect of learning curve on short-term outcomes. a meta-analysis. J Laparoendosc Adv Surg Tech A 24: 139-150, 2014

13. Hu WG, Ma JJ, Zang L, et al: Learning curve and long-term outcomes of laparoscopy-assisted distal gastrectomy for gastric cancer. J Laparoendosc Adv Surg Tech A 24:487-492, 2014

14. Kim CY, Nam BH, Cho GS, et al: Learning curve for gastric cancer surgery based on actual survival. Gastric Cancer, 2015 [epub ahead of print on February 25, 2015]

15. Park EJ, Kim MS, Kim G, et al: Long-term oncologic outcomes of laparoscopic right hemicolectomy during the learning curve period: Comparative study with cases after the learning curve period. Surg Laparosc Endosc Percutan Tech 25: 52-58, 2015

16. Sutton DN, Wayman J, Griffin SM: Learning curve for oesophageal cancer surgery. Br J Surg 85: 1399-1402, 1998

17. Mackenzie H, Markar SR, Askari A, et al: The national proficiency-gain curves for minimal access gastrointestinal cancer surgery. Br J Surg 103:88-96, 2016

18. van der Schaaf M, Johar A, Wijnhoven B, et al: Extent of lymph node removal during esophageal cancer surgery and survival. J Natl Cancer Inst 107: djv043, 2015

19. Barlow L, Westergren K, Holmberg L, et al: The completeness of the Swedish Cancer Register: A sample survey for year 1998. Acta Oncol 48:27-33, 2009

20. Lindblad M, Ye W, Lindgren A, et al: Disparities in the classification of esophageal and cardia adenocarcinomas and their influence on reported incidence rates. Ann Surg 243:479-485, 2006

21. Lagergren K, Derogar M: Validation of oesophageal cancer surgery data in the Swedish Patient Registry. Acta Oncol 51:65-68, 2012

22. Charlson ME, Pompei P, Ales KL, et al: A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis 40:373-383, 1987

23. Lagergren J, Bergström R, Lindgren A, et al: Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. N Engl J Med 340: 825-831, 1999

24. Rouvelas I, Zeng W, Lindblad M, et al: Survival after surgery for oesophageal cancer: A population-based study. Lancet Oncol 6:864-870, 2005

25. Sobin LH, Gospodarowicz MK, Wittekind C (eds). UICC TNM classification of malignant tumors. 7th ed. Wiley Blackwell, Hoboken, NJ, 2009.

26. Grigg OA, Farewell VT, Spiegelhalter DJ: Use of risk-adjusted CUSUM and RSPRT charts for monitoring in medical contexts. Stat Methods Med Res 12:147-170, 2003

27. Markar SR, Gronnier C, Duhamel A, et al: Significance of microscopically incomplete resection margin after esophagectomy for esophageal cancer. Ann Surg 2015 [Epub ahead of print on December 12, 2015]

28. van der Schaaf M, Derogar M, Johar A, et al: Reoperation after esophageal cancer surgery in relation to long-term survival: A population-based cohort study. BMJ Open 4:e004648, 2014

29. Mackenzie H, Cuming T, Miskovic D, et al: Design, delivery, and validation of a trainer curriculum for the national laparoscopic colorectal training program in England. Ann Surg 261: 149-156, 2015

30. Mackenzie H, Ni M, Miskovic D, et al: Clinical validity of consultant technical skills assessment in the English National Training Programme for Laparoscopic Colorectal Surgery. Br J Surg 102:991-997, 2015

31. Coleman MG, Hanna GB, Kennedy R: The National Training Programme for Laparoscopic Colorectal Surgery in England: A new training paradigm. Colorectal Dis 13:614-616, 2011

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Surgical Proficiency Gain and Survival After Esophagectomy for Cancer

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or jco.ascopubs.org/site/ifc.

Sheraz R. Markar
No relationship to disclose

Hugh Mackenzie
No relationship to disclose

Pernilla Lagergren
No relationship to disclose

George B. Hanna
No relationship to disclose

Jesper Lagergren
No relationship to disclose

Appendix

Table A1. Sample Logistic Regression Analysis Used For Risk-Adjusted CUSUM Analysis of All-Cause 30-Day Mortality

	Analysis Data		
Variable at step 1	*P*	OR	95% CI for OR
Age at operation	.000	.936	.911 to .961
Sex	.310	.764	.454 to 1.285
Histology	.001	2.249	1.387 to 3.646
Stage	.738		
I	.220	2.104	.641 to 6.901
II	.439	1.459	.560 to 3.799
III	.687	1.172	.541 to 2.539
IV	.510	1.304	.591 to 2.877
Neoadjuvant therapy	.915	.973	.584 to 1.620
Ischemic heart disease	.124	1.631	.874 to 3.041
Congestive cardiac failure	.029	2.110	1.078 to 4.132
Peripheral vascular disease	.091	1.989	.897 to 4.412
Cerebrovascular disease	.426	1.331	.658 to 2.692
Chronic pulmonary disease	.445	.760	.376 to 1.536
Diabetes	.055	1.906	.986 to 3.683
Liver disease	.693	.657	.082 to 5.286
Renal disease	.038	4.009	1.081 to 14.871
Constant	.028	41.580	

Abbreviation: OR, odds ratio.